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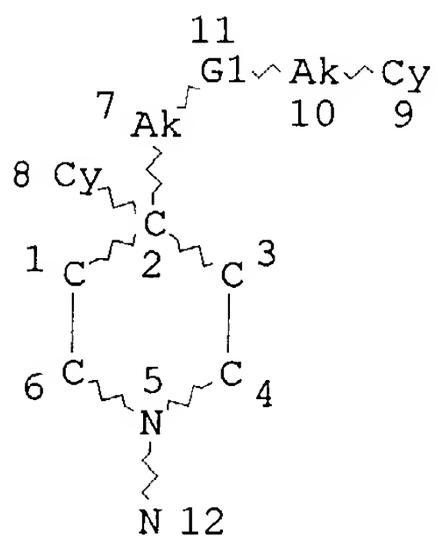
L1 HAS NO ANSWERS
L1 STR



VAR G1=O/S/N
NODE ATTRIBUTES:
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GGCAT IS MCY UNS AT 8
GGCAT IS MCY UNS AT 9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 2
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

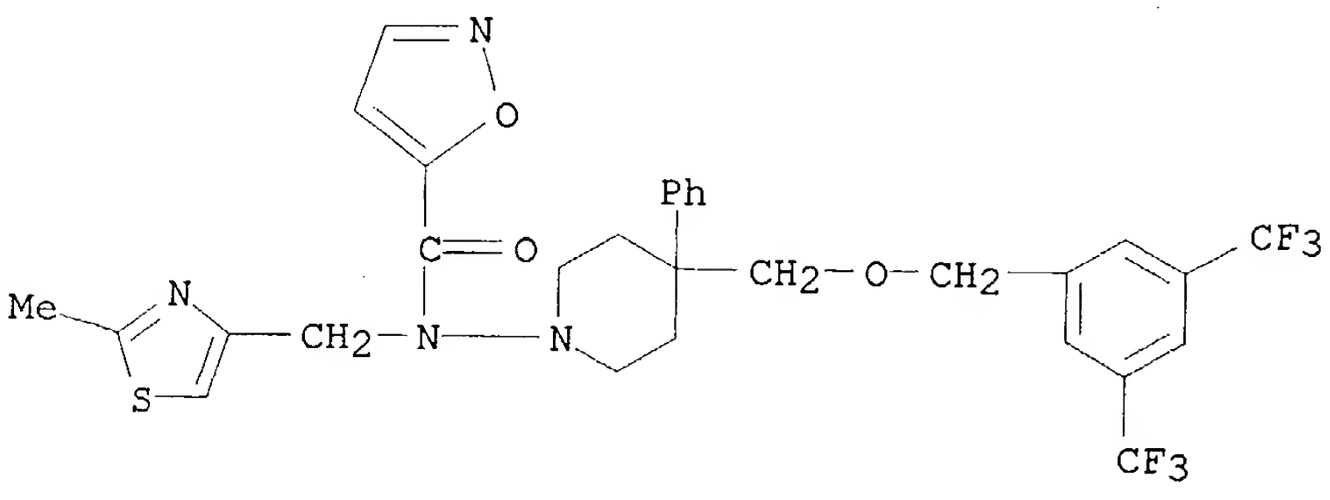
=> s l1 ful
FULL SEARCH INITIATED 15:17:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 58642 TO ITERATE

100.0% PROCESSED 58642 ITERATIONS 53 ANSWERS
SEARCH TIME: 00.00.02

L3 53 SEA SSS FUL L1

=> d scan

L3 53 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 5-Isoxazolecarboxamide, N-[4-[[[3,5-bis(trifluoromethyl)phenyl]methoxy]met
hyl]-4-phenyl-1-piperidinyl]-N-[(2-methyl-4-thiazolyl)methyl]- (9CI)
MF C30 H28 F6 N4 O3 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	157.10	157.31

FILE 'CAPLUS' ENTERED AT 15:17:58 ON 18 OCT 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 18 Oct 2004 VOL 141 ISS 17
FILE LAST UPDATED: 17 Oct 2004 (20041017/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 1 L3

=> d bib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41271 CAPLUS
DN 140:93933
TI Preparation of 1-amido-4-phenyl-4-benzyloxymethylpiperidine derivatives and related compounds as neurokinin-1 (NK-1) antagonists for the treatment of emesis, depression, anxiety and cough
IN Shih, Neng-Yang; Wang, Steven; Reichard, Gregory A.; Xiao, Dong; Wang, Cheng
PA Schering Corporation, USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004722	A1	20040115	WO 2003-US20783	20030702

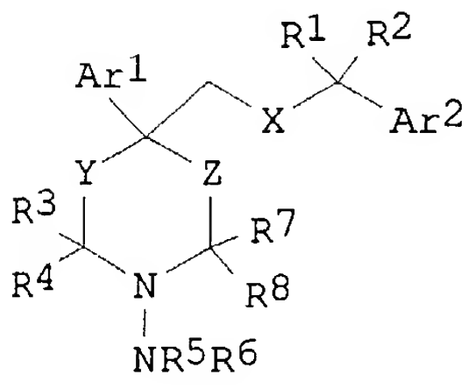
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2004072867	A1	20040415	US 2003-612176	20030702
PRAI	US 2002-393708P	P	20020703		

OS MARPAT 140:93933

GI



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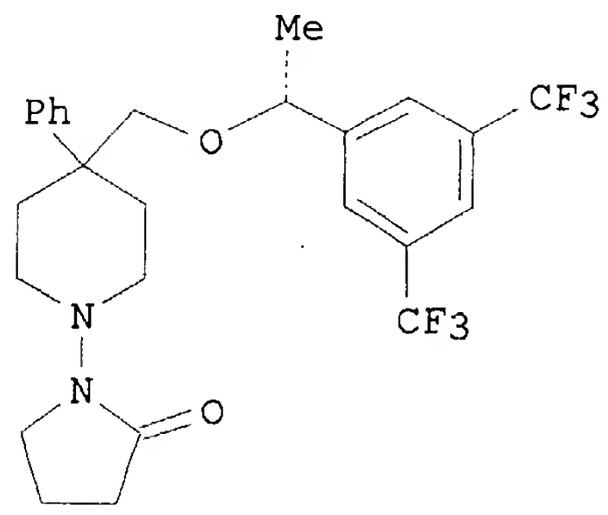

II

AB The title compds. of formula I [Ar1, Ar2 = (substituted) Ph, (substituted) heteroaryl; R1, R3 = H, alkyl, oxo; R2, R4 = H, (substituted) CONH2, etc.; R5, R6 = H, alkyl, cycloalkyl, aryl, etc.; R5R6 = heterocyclo ring, etc.; R7, R8 = H, alkyl, oxo; X = O, S, (substituted) NH, SO, SO2; Y = (CH2)m; Z = (CH2)n; m, n = 0-3 (m+n = 0-4)] are prepared as NK1 antagonists. The compds. are useful for treating disorders, symptoms or diseases, including emesis, depression, anxiety and cough. Thus, II was prepared, and had Ki of 0.3 nM in NK1 binding assay.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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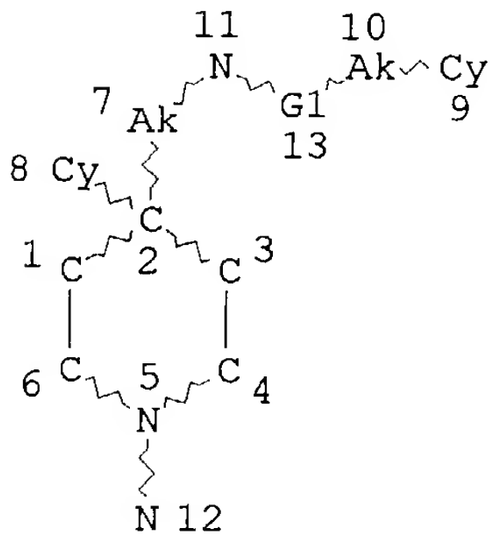
L5 HAS NO ANSWERS
L5 STR



VAR G1=C/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 8
GGCAT IS MCY UNS AT 9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 2
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE

=> s l5 ful
FULL SEARCH INITIATED 15:20:34 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 60212 TO ITERATE

100.0% PROCESSED 60212 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.02

L7 0 SEA SSS FUL L5

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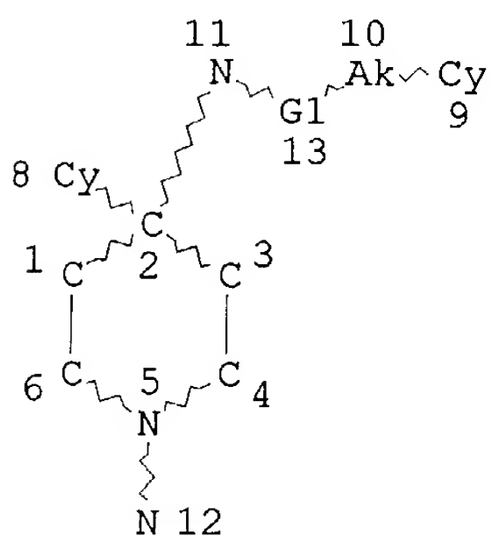
L8 HAS NO ANSWERS
L8 STR



VAR G1=C/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 8
GGCAT IS MCY UNS AT 9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 2
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

=> s l8 ful
FULL SEARCH INITIATED 15:21:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2606 TO ITERATE

100.0% PROCESSED 2606 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L10 0 SEA SSS FUL L8

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L11 HAS NO ANSWERS
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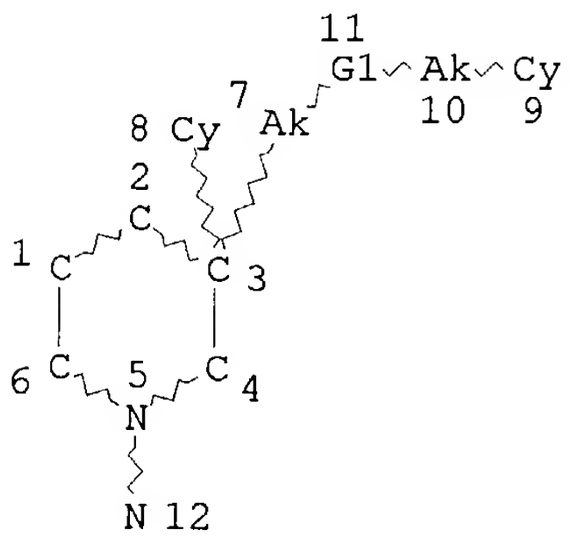


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VAR G1=O/S/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY  UNS  AT   8
GGCAT   IS MCY  UNS  AT   9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   3
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE


=> s l11 ful
FULL SEARCH INITIATED 15:23:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  58642 TO ITERATE

100.0% PROCESSED   58642 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L13             0 SEA SSS FUL L11
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=> s nk1(l)(cough or depression or anxiety or emesis)
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          4305 COUGH
         70665 DEPRESSION
         12008 ANXIETY
          2448 EMESIS
L1         273 NK1(L)(COUGH OR DEPRESSION OR ANXIETY OR EMESIS)

=> s l1(l)piperidin?
         87778 PIPERIDIN?
L2          39 L1(L)PIPERIDIN?

=> s l2(l)pyrrol?
        130231 PYRROL?
L3           9 L2(L)PYRROL?

=> d bib abs 1-9

L3   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:550949  CAPLUS
DN   141:106497
TI   Preparation of substituted 1-piperidin-4-yl-4-azetidin-3-yl-piperazine
     derivatives and their use as neurokinin antagonists
IN   Janssens, Frans Eduard; Sommen, Francois Maria; De Boeck, Benoit Christian
     Albert Ghislain; Leenaerts, Joseph Elisabeth
PA   Janssen Pharmaceutica N.V., Belg.
SO   PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ----------          ----   --------    -------------------      --------
PI   WO 2004056800        A1    20040708    WO 2003-EP51042          20031217
        W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
            NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
            TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM,
            AZ, BY, KG, KZ
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
            BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
            MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
            GQ, GW, ML, MR, NE, SN, TD, TG
PRAI WO 2002-EP14837      A     20021223
OS   MARPAT 141:106497
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

AB   Title compds. I [Q = O or NR3; X = covalent bond, -O-, -S-, or -NR3; R1
     independently = Ar1, Ar1-alkyl, and di(Ar1)-alkyl; R2 = Ar2, Ar2-alkyl,
     di(Ar2)-alkyl Het1, Het1-alkyl; R3 independently = H or alkyl; Y =
     covalent bond, -CO-, -SO2-, >C:CHR or >C:NR, wherein R = H, CN or NO2; M
     independently = covalent bond, (un)substituted-alkyl, -(un)saturated
     carbocycle; L = H, alkyloxy, Ar3oxy, alkylamine, etc.; Ar1 =
     (un)substituted phenyl; Ar2 = (un)substituted naphthalenyl or Ph with
```

substituent(s) selected from halo, alkyl, CN, aminocarbonyl, and alkyloxy; Ar3 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, amino, alkyloxy, OH, pyridinyl, etc.; Het1 = monocyclic heterocyclic radical selected from **pyrrolyl**, pyrazolyl, imidazolyl, furanyl, etc.; m = 1 or 2 provided that if m = 2, then n = 1; n = 0-2; p = 1-2; q = 0-1] and their pharmaceutically acceptable salts having neurokinin antagonistic activity, in particular **NK1** antagonistic activity and **NK1**/NK3- antagonistic activity, their preparation, compns. comprising them and their use as a medicine, in particular for the treatment of schizophrenia, **emesis**, **anxiety**, **depression**, irritable bowel syndrome (IBS), circadian rhythm disturbances, pain, neurogenic inflammation, asthma, micturition disorders such as urinary incontinence and nociception are disclosed. Thus, e.g., II was prepared by reaction of (2R-trans)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(1-piperazinyl) **piperidine** (preparation given) with 1-(diphenylmethyl)-3-azetidinyl methanesulfonate. For selected compds. of the invention, receptor binding pIC50 values for h-**NK1** were in a range from 6.69-8.13. In view of their capability to antagonize the actions of tachykinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P by blocking the NK receptors, the compds. according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin mediated conditions, such as, for instance CNS disorders, in particular **depression**, **anxiety** disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, schizoaffective disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS related conditions ; inflammation ; allergic disorders ; **emesis** ; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders ; vasospastic diseases ; fibrosing and collagen diseases ; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:550948 CAPLUS
DN 141:106496
TI Preparation of substituted 1-piperidin-4-yl-4-pyrrolidin-3-yl-piperazine derivatives and their use as neurokinin antagonists
IN Janssens, Frans Eduard; Sommen, Francois Maria; De Boeck, Benoit Christian Albert Ghislain; Leenaerts, Joseph Elisabeth
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004056799	A2	20040708	WO 2003-EP51041	20031217
WO 2004056799	A3	20040812		

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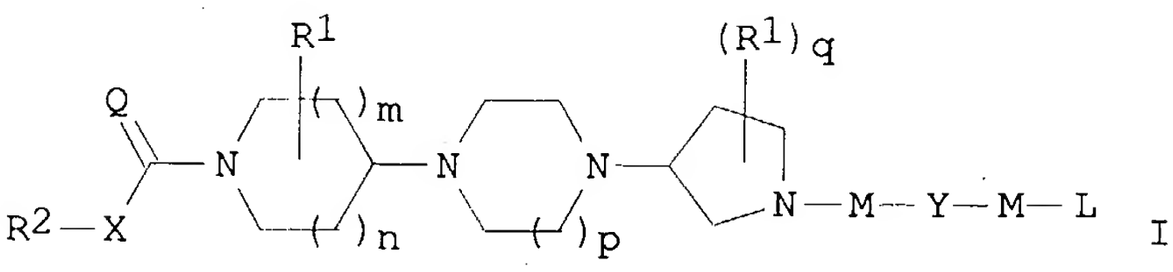
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,

MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2002-EP14831 A 20021223

OS MARPAT 141:106496

GI



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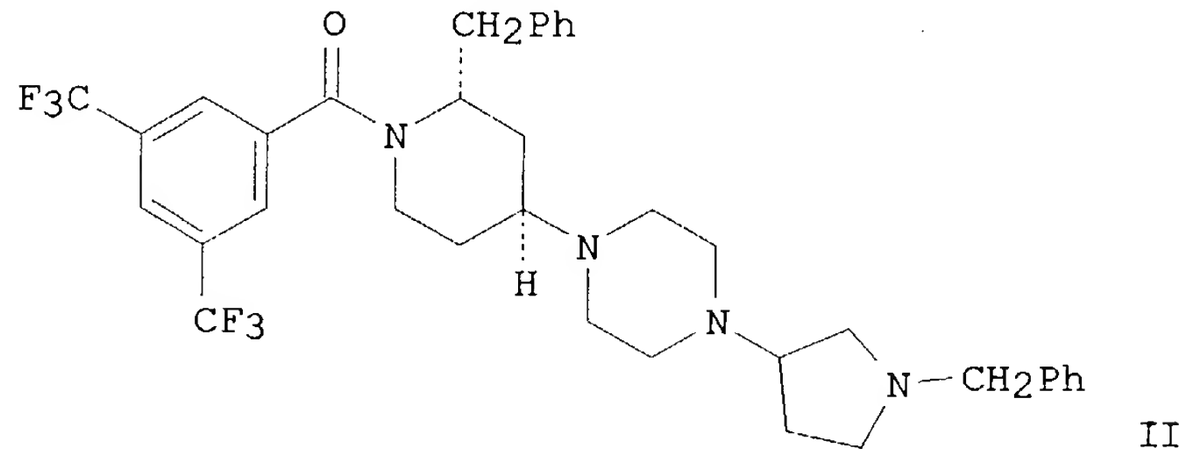

II

AB Title compds. I [Q = O or NR3; X = covalent bond, -O-, -S-, or -NR3; R1 independently = Ar1, Ar1-alkyl, and di(Ar1)-alkyl; R2 = Ar2, Ar2-alkyl, di(Ar2)-alkyl Het1, Het1-alkyl; R3 independently = H or alkyl; Y = covalent bond, -CO-, -SO2-, >C:CHR or >C:NR, wherein R = H, CN or NO2; M independently = covalent bond, (un)substituted-alkyl, -(un)saturated carbocycle; L = H, alkyloxy, Ar3oxy, alkylamine, etc.; Ar1 = (un)substituted phenyl; Ar2 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, aminocarbonyl, and alkyloxy; Ar3 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, amino, alkyloxy, OH, pyridinyl, etc.; Het1 = monocyclic heterocyclic radical selected from **pyrrolyl**, pyrazolyl, imidazolyl, furanyl, etc.; m = 1 or 2 provided that if m = 2, then n = 1; n = 0-2; p = 1-2; q = 0-1] and their pharmaceutically acceptable salts having neurokinin antagonistic activity, in particular **NK1** antagonistic activity, a combined **NK1**/NK3 antagonistic activity and a combined **NK1**/NK2/NK3 antagonistic activity, their preparation, compns. comprising them and their use as a medicine, in particular for the treatment of schizophrenia, **anxiety**, **depression**, **emesis** and IBS are disclosed. Thus, e.g., II was prepared by reaction of (2R-trans) 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(1-piperazinyl)**piperidine** (preparation given) and 1-(phenylmethyl)-3-**pyrrolidinone**. The receptor binding values (pIC50) for the h-**NK1** ranges for all compds. according to the invention between 10 and 6. In view of their capability to antagonize the actions of tachykinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P and Neurokinin B by blocking the **NK1**, NK2 and NK3 receptors, the compds. according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin-mediated conditions, such as, for instance CNS disorders, in particular schizoaffective disorders, **depression**, **anxiety** disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, eating disorders, neurodegenerative diseases,

addiction disorders, mood disorders, sexual dysfunction, pain and other CNS-related conditions ; inflammation ; allergic disorders ; **emesis** ; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders ; vasospastic diseases ; fibrosing and collagen diseases ; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

L3 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:550876 CAPLUS
DN 141:106495
TI Substituted 1-piperidin-3-yl-4-piperidin-4-yl-piperazine derivatives and their use as neurokinin antagonists
IN Janssens, Frans Eduard; Sommen, Francois Maria; De Boeck, Benoit Christian Albert Ghislain; Leenaerts, Joseph Elisabeth
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004056364	A1	20040708	WO 2003-EP51035	20031217
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	WO 2002-EP14835	A	20021223		

OS MARPAT 141:106495
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Q = O or NR3; X = covalent bond, -O-, -S-, or -NR3; R1 independently = Ar1, Ar1-alkyl, and di(Ar1)-alkyl; R2 = Ar2, Ar2-alkyl, di(Ar2)-alkyl Het1, Het1-alkyl; R3 independently = H or alkyl; Y = covalent bond, -CO-, -SO2-, >C:CHR or >C:NR, wherein R = H, CN or NO2; M independently = covalent bond, (un)substituted-alkyl, -(un)saturated carbocycle; L = H, alkyloxy, Ar3oxy, alkylamine, etc.; Ar1 = (un)substituted phenyl; Ar2 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, aminocarbonyl, and alkyloxy; Ar3 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, amino, alkyloxy, OH, pyridinyl, etc.; Het1 = monocyclic heterocyclic radical selected from **pyrrolyl**, pyrazolyl, imidazolyl, furanyl, etc.; m = 1 or 2 provided that if m = 2, then n = 1; n = 0-2; p = 1-2; q = 0-1] and their pharmaceutically acceptable salts having neurokinin antagonistic activity, in particular **NK1** antagonistic activity, a combined **NK1**/NK3 antagonistic activity and a combined **NK1**/NK2/NK3 antagonistic activity, their preparation, compns. comprising them and their use as a medicine, in particular for the treatment of schizophrenia, **emesis**, **anxiety** and **depression**, irritable bowel syndrome (IBS), circadian rhythm

disturbances, visceral pain, neurogenic inflammation, asthma, micturition disorders such as urinary incontinence and nociception are disclosed. Thus, e.g., II was prepared via reaction of (2R-trans)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(1-piperazinyl) **piperidine** (preparation given) with 1-(phenylmethyl)-3-**piperidinone**. The receptor binding values (pIC50) for the h-**NK1** ranges for all compds. according to the invention between 10 and 6. In view of their capability to antagonize the actions of tachykinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P, Neurokinin A and Neurokinin B by blocking the **NK1**, NK2 and NK3 receptors, the compds. according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin-mediated conditions, such as, for instance CNS disorders, in particular schizoaffective disorders, **depression**, **anxiety** disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS-related conditions; inflammation; allergic disorders; **emesis**; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders; vasospastic diseases; fibrosing and collagen diseases; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:546478 CAPLUS
DN 141:89116
TI Preparation of substituted 1,4-di-piperidin-4-yl-piperazine derivatives and their use as tachykinin antagonists
IN Janssens, Frans Eduard; Sommen, Francois Maria; De Boeck, Benoit Christian Albert Ghislain; Leenaerts, Joseph Elisabeth; Van Roosbroeck, Yves Emiel Maria
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004056772	A1	20040708	WO 2002-EP14836	20021223
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004033428	A1	20040422	WO 2003-EP50697	20031007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2002-EP11328 A 20021008
WO 2002-EP14836 A 20021223

OS MARPAT 141:89116

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Tile compds. I [Q = O or NR3; X = covalent bond, -O-, -S-, or -NR3; R1 independently = Ar1, Ar1-alkyl, and di(Ar1)-alkyl; R2 = alkyl, Ar2, Ar2-alkyl, Het1, Het1-alkyl; R3 independently = H or alkyl; Y = covalent bond, CO, SO2; M independently = covalent bond, (un)substituted-alkyl, -(un)saturated carbocycle; L = H, alkyloxy, Ar3oxy, alkylamine, etc.; Ar1 = (un)substituted phenyl; Ar2 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, aminocarbonyl, and alkyloxy; Ar3 = (un)substituted naphthalenyl or Ph with substituent(s) selected from halo, alkyl, CN, amino, alkyloxy, OH, pyridinyl, etc.; Het1 = monocyclic heterocyclic radical selected from **pyrrolyl**, pyrazolyl, imidazolyl, furanyl, etc.; m = 1 or 2 provided that if m = 2, then n = 1; n = 0-2; p = 1-2; q = 0-1] and their pharmaceutically acceptable salts are disclosed as having tachykinin antagonistic activity, in particular **NK1** antagonistic activity. Their preparation, compns. comprising them and their use as a medicine, in particular for the treatment of **emesis**, **anxiety**, **depression** and irritable bowel syndrome (IBS) are disclosed. Thus, II was prepared via resolution of III (preparation given), de-N-benzylation, and reaction with 1-(phenylmethyl)-4-**piperidinone**. Selected compds. of the invention were evaluated for binding to h-**NK1**, h-NK2, and h-NK3 receptors with all compds. showing (sub)nanomolar affinity for h-**NK1** with most possessing more than 100-fold selectivity towards the h-NK2 and h-NK3 receptors. In view of their capability to antagonize the actions of tachykinins by blocking the tachykinin receptors, and in particular antagonizing the actions of substance P by blocking the **NK1** receptor, the compds. according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin-mediated conditions, such as, for instance CNS disorders, in particular **depression**, **anxiety** disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, schizoaffective disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS-related conditions; inflammation; allergic disorders; **emesis**; gastrointestinal disorders, in particular IBS; skin disorders; vasospastic diseases; fibrosing and collagen diseases; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.

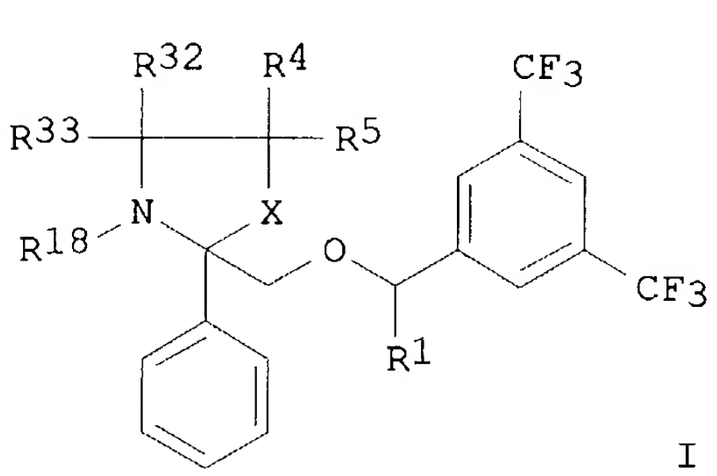
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:491186 CAPLUS
DN 139:69145
TI Preparation of pyrrolidine and piperidine derivatives for therapeutic use as neurokinin 1 (NK1) receptor antagonists
IN Paliwal, Sunil; Reichard, Gregory A.; Wang, Cheng; Xiao, Dong; Tsui, Hon-Chung; Shih, Neng-Yang; Arredondo, Juan D.; Wrobleski, Michelle Laci; Palani, Anandan

PA Schering Corporation, USA
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003051840	A1	20030626	WO 2002-US40203	20021217
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003158173	A1	20030821	US 2002-321687	20021217
	EP 1463716	A1	20041006	EP 2002-805167	20021217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI	US 2001-341452P	P	20011218		
	WO 2002-US40203	W	20021217		

OS MARPAT 139:69145
GI



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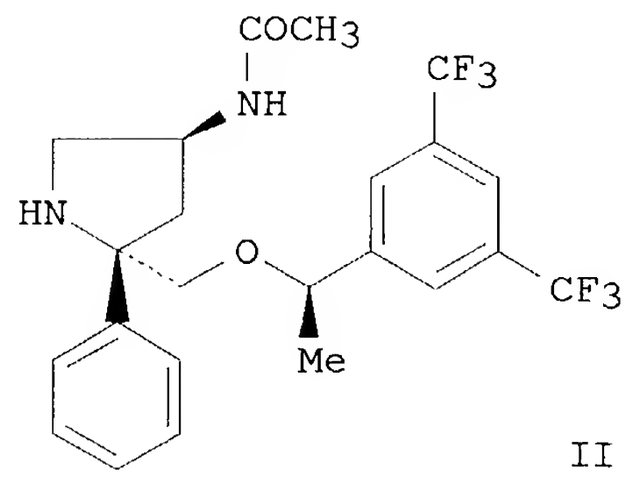


II

AB **Pyrrolidine** and **piperidine** derivs., such as I [X = (CR6R7)n; n = 1, 2; R1 = H, alkyl, etc.; R4, R5, R6, R7,R32, R33 = H or radical, such as amino, alkyl, alkoxy, acyl, or heterocyclyl; R4R5 = :O, oxime, spiro bonded nitrogen containing ring, etc.], were prepared for use in pharmaceutical compns. as **NK1** receptor antagonists. These **pyrrolidine** and **piperidine** derivs. are intended for use in the treatment of a number of disorders, including **emesis**, **depression**, **anxiety**, respiratory disease, **cough**, inflammatory disease, skin disorder, ophthalmalogical disorder, **depression**, **anxiety**, phobia, bipolar disorder, alc. dependence, psychoactive substance abuse, epilepsy, nociception, psychosis, schizophrenia, Alzheimer's disease, AIDS related dementia, Towne's disease, stress related disorder, obsessive/compulsive disorder, bulimia, anorexia nervosa, binge eating, mania, premenstrual syndrome, gastrointestinal disorder, atherosclerosis, fibrosing disorder, obesity, Type II diabetes, headache, neuropathic pain, postoperative pain, chronic pain syndrome, bladder disorder, genitourinary disorder or migraine. Thus, **pyrrolidine** derivative II was prepd via a multistep synthetic sequence which began with an alkylation reaction of (2R,4S)-5-oxo-2,4-diphenyl-3-oxazolidinecarboxylic acid phenylmethyl ester with

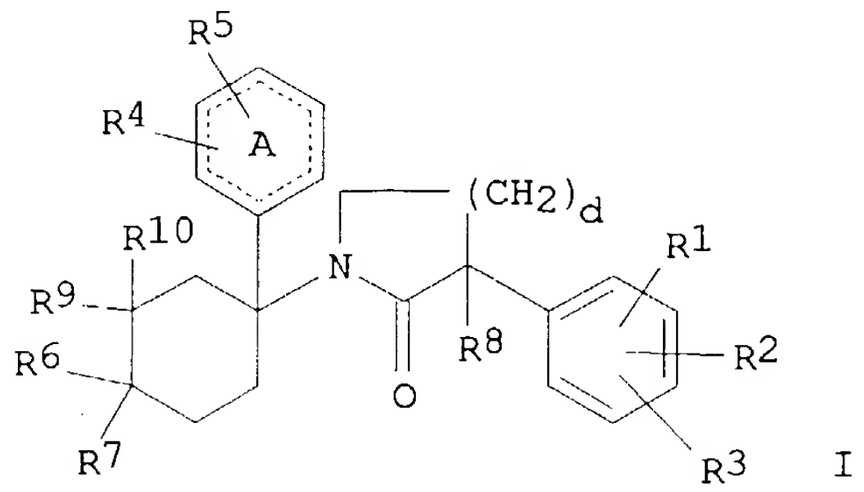
1-[(1R)-1-(bromomethoxy)ethyl]-3,5-bis(trifluoromethyl)benzene. The prepared **pyrrolidine** and **piperidine** derivs. were tested for **NK1** receptor binding activity.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:977652 CAPLUS
DN 138:55871
TI Preparation of gem-disubstituted cyclohexane-containing azetidinones, pyrrolidinones and piperidinones as neurokinin 1 receptor antagonists and their use as therapeutic agents
IN Castro Pineiro, Jose Luis; Dinnell, Kevin; Elliott, Jason Matthew; Hollingworth, Gregory John; Shaw, Duncan Edward; Swain, Christopher John
PA Merck Sharp & Dohme Limited, UK
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002102372	A1	20021227	WO 2002-GB2654	20020610
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004171642	A1	20040902	US 2003-481477	20031217
PRAI	GB 2001-14867	A	20010618		
	WO 2002-GB2654	W	20020610		

OS MARPAT 138:55871
GI



I

AB The present invention relates to gem-disubstituted cyclohexane-containing azetidinones, **pyrrolidinones** and **piperidinones** (shown as I; e.g. 3-[3,5-bis(trifluoromethyl)phenyl]-1-(1,4-dioxa-8-phenylspiro[4.5]decan-8-yl)-2-**piperidinone**; R1, R2, R3, R4, R5, R6, R7, R8, R9 and R10 = a variety of substituents; ring A is a Ph or pyridyl ring; d is 0-2) and pharmaceutically acceptable salts and N-oxides thereof. The compds. are of particular use in the treatment or prevention of **depression**, **anxiety**, pain, inflammation, migraine, **emesis** or post-therapeutic neuralgia. The compds. are active with

IC50 at the **NK1** receptor of <100nM on said test method. In the treatment of the conditions associated with an excess of tachykinins, a suitable dosage level is .apprx.0.001-50 mg/kg per day, in particular .apprx.0.01 to .apprx.25 mg/kg, such as from .apprx.0.05 to .apprx.10 mg/kg per day. For example, in the treatment of conditions involving the neurotransmission of pain sensations, a suitable dosage level is .apprx.0.001-25 mg/kg per day, preferably .apprx.0.005-10 mg/kg per day, and especially .apprx.0.005-5 mg/kg per day. In the treatment of **emesis** or psychiatric disorders, a suitable dosage level is .apprx.0.001-10 mg/kg per day, preferably .apprx.0.005-5 mg/kg per day, and especially 0.01-3 mg/kg per day. The compds. may be administered on a regimen of 1-4 times per day, preferably once or twice per day. Although the methods of preparation are not claimed, 26 example intermediate and 23 example claimed compound prepns. are included.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:753212 CAPLUS
DN 132:3369
TI Carboxy substituted carboxamide derivatives as tachykinin receptor antagonists
IN Burkholder, Timothy P.; Maynard, George L.; Kudlacz, Elizabeth M.
PA Hoechst Marion Roussel, Inc., USA
SO PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959972	A1	19991125	WO 1999-US9450	19990430
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2329075	AA	19991125	CA 1999-2329075	19990430
	AU 9937756	A1	19991206	AU 1999-37756	19990430
	AU 743487	B2	20020124		
	EP 1077942	A1	20010228	EP 1999-920201	19990430
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002515487	T2	20020528	JP 2000-549591	19990430
	NZ 507432	A	20030829	NZ 1999-507432	19990430
	CN 1136190	B	20040128	CN 1999-806189	19990430
	US 6316445	B1	20011113	US 1999-648005	19990506
	NO 2000005756	A	20010112	NO 2000-5756	20001114
	ZA 2000006606	A	20020214	ZA 2000-6606	20001114
PRAI	US 1998-79610	A	19980515		
	US 1998-126447P	P	19980515		
	WO 1999-US9450	W	19990430		

OS MARPAT 132:3369
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to novel carboxy-substituted acyclic carboxamide derivs. of formula I, and stereoisomers and pharmaceutically acceptable salts thereof, as well as their use as tachykinin receptor antagonists [wherein R1 = 1-3 of H, halo, C1-6 alkyl or alkoxy; R2 = H, 4H-1,2,4-triazol-4-yl, or 1H-tetrazol-1-yl bearing optional CF3 or C1-4 alkyl in 5-position; Ar1 = (un)substituted Ph, naphthyl, pyridyl, or thienyl; Ar2 = (un)substituted Ph or pyridyl; X = carboxy-bearing derivs. of **pyrrolidino**, **piperidino**, morpholino, or piperazino, or their C1-6 alkyl esters]. Such antagonists are useful in the treatment of tachykinin-mediated diseases and conditions disclosed herein, including in particular asthma, **cough**, and bronchitis. For example, the title compound II was prepared by reductive amination of the aldehyde III by **piperidine** derivative IV.HI using NaBH3CN in MeOH. The intermediates III and IV were prepared in sequences of 8 and 2 steps, resp. The HCl salt of II inhibited binding of radioligands to **NK1** and NK2 receptors with IC50 values of 23 nM and 178 nM, resp.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:424246 CAPLUS
DN 129:95499
TI Novel heterocyclic substituted pyrrolidine amide derivatives useful as tachykinin receptor antagonists
IN Burkholder, Thimothy P.; Maynard, George D.; Kudlacz, Elizabeth M.
PA Hoechst Marion Roussel, Inc., USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9827086	A1	19980625	WO 1997-US19884	19971103
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851607	A1	19980715	AU 1998-51607	19971103
AU 723966	B2	20000907		
EP 946548	A1	19991006	EP 1997-946443	19971103
EP 946548	B1	20020306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1241185	A	20000112	CN 1997-180825	19971103
CN 1119344	B	20030827		
BR 9714057	A	20000509	BR 1997-14057	19971103
NZ 335975	A	20001124	NZ 1997-335975	19971103
JP 2001506650	T2	20010522	JP 1998-527682	19971103
AT 214063	E	20020315	AT 1997-946443	19971103
PT 946548	T	20020628	PT 1997-946443	19971103
ES 2169881	T3	20020716	ES 1997-946443	19971103
CA 2275527	C	20030923	CA 1997-2275527	19971103
ZA 9711271	A	19980619	ZA 1997-11271	19971215
TW 486477	B	20020511	TW 1997-86119004	19971216
NO 9903013	A	19990818	NO 1999-3013	19990618
KR 2000057668	A	20000925	KR 1999-705496	19990618

	HK 1020947	A1	20020816	HK 1999-106022	19991221
PRAI	US 1996-769812	A	19961219		
	WO 1997-US19884	W	19971103		

OS MARPAT 129:95499
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to novel heterocyclic substituted **pyrrolidine** amide derivs. I and stereoisomers and pharmaceutically acceptable salts thereof [wherein R1 = 1-3 of H, halo, CF3, alkyl, alkoxy; R2 = H, alkyl, alkoxy; R3 = 1-tetrazolyl or its 5-alkyl or 5-CF3 derivs., 1,2,4-triazol-4-yl; Ar = C6H4R5 or -pyridyl-R6; R5 = 1-3 of H, halo, CF3, alkyl, or alkoxy; R6 = 1-2 of H, halo, alkyl, or alkoxy; R7, R8 = H; or NR7R8 = **piperidine**, morpholine, piperazine, 4-methylpiperazine, or **pyrrolidine** ring]. As tachykinin receptor antagonists, the compds. are useful in the treatment of tachykinin-mediated diseases and conditions, including particularly asthma, **cough**, and bronchitis. For instance, the salt of (S)-3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)**pyrrolidine** with (R,R)-di-p-anisoyltartaric acid underwent a sequence of N-protection as the BOC derivative, O-mesylation, coupling of the mesylate with 4-phenylpiperidine-4-carboxylic acid amide hydrochloride, N-deprotection, amidation with 2-methoxy-5-(1H-tetrazol-1-yl)benzoic acid, and acidification, to give title compound II as the hydrochloride. The latter bound to **NK1** and NK2 receptors in vitro with IC50 values of 2.79 nM and 16.3 nM, resp. This compound showed both higher **NK1** selectivity and higher metabolic stability in comparison to a known compound of similar structure.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:424245 CAPLUS
DN 129:95498
TI Novel heterocyclic carboxy-substituted cyclic carboxamide derivatives useful as tachykinin receptor antagonists
IN Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elisabeth M.
PA Hoechst Marion Roussel, Inc., USA
SO PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9827085	A1	19980625	WO 1997-US21586	19971121
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5977139	A	19991102	US 1997-971891	19971117
	AU 9853627	A1	19980715	AU 1998-53627	19971121
	AU 718984	B2	20000504		
	EP 946545	A1	19991006	EP 1997-950690	19971121
	EP 946545	B1	20010905		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

	CN 1240443	A	20000105	CN 1997-180774	19971121
	CN 1098259	B	20030108		
	BR 9714156	A	20000208	BR 1997-14156	19971121
	NZ 335883	A	20010727	NZ 1997-335883	19971121
	AT 205200	E	20010915	AT 1997-950690	19971121
	ES 2162686	T3	20020101	ES 1997-950690	19971121
	PT 946545	T	20020228	PT 1997-950690	19971121
	JP 2002512596	T2	20020423	JP 1998-527720	19971121
	RU 2199535	C2	20030227	RU 1999-115883	19971121
	CA 2275602	C	20030722	CA 1997-2275602	19971121
	EE 4117	B1	20030815	EE 1999-254	19971121
	ZA 9711264	A	19980623	ZA 1997-11264	19971215
	TW 544452	B	20030801	TW 1997-86119362	19971219
	NO 9903012	A	19990818	NO 1999-3012	19990618
	KR 2000057667	A	20000925	KR 1999-705495	19990618
	HK 1020571	A1	20020517	HK 1999-105551	19991130
PRAI	US 1996-794157	A	19961219		
	US 1997-971891	A	19971117		
	WO 1997-US21586	W	19971121		

OS MARPAT 129:95498

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to novel carboxy-substituted cyclic carboxamide derivs. I and stereoisomers and pharmaceutically acceptable salts thereof [wherein either G1 or G2 = CH2, while other = CO; m = 2 or 3; n = 0 or 1; R1 = 1-3 of H, halo, CF3, alkyl, alkoxy; R2 = 1-3 of H, halo, cyano, CF3, alkyl, alkoxy; R3 = 1-tetrazolyl or its 5-alkyl or 5-CF3 derivs., 1,2,4-triazol-4-yl, 1H-tetrazol-5-yl; Ar = (un)substituted Ph or pyridyl; A = carboxy- or carboxy-derivative-substituted **pyrrolidino**, piperazino, morpholino, thiomorpholino or oxides, or **piperidino**]. As tachykinin receptor antagonists, the compds. are useful in the treatment of tachykinin-mediated diseases and conditions, including particularly asthma, **cough**, and bronchitis. For instance, (S)-3-(3,4,5-trimethoxybenzoyl)-3-(3,4-dichlorophenyl)-3-(2-methanesulfonyloxyethyl)**pyrrolidine** was condensed with 4-phenyl-4-[[(S)-2-carbomethoxypyrrolidin-1-yl]carboxamido] **piperidine** hydriodide to give title compound II. The latter bound to **NK1** and NK2 receptors in vitro with IC50 values of 4.32 nM and 4.51 nM, resp.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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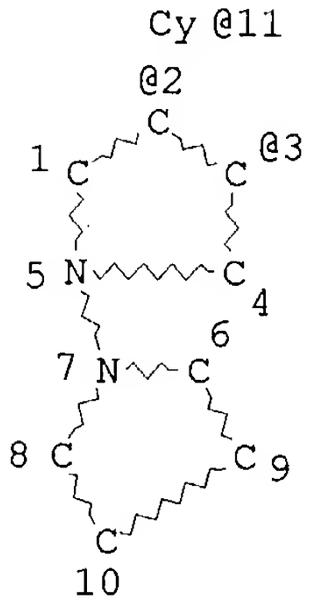

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 4 7
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

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FULL SEARCH INITIATED 15:38:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 8685 TO ITERATE

100.0% PROCESSED 8685 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

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FULL ESTIMATED COST	156.26	156.47

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FILE COVERS 1907 - 18 Oct 2004 VOL 141 ISS 17

FILE LAST UPDATED: 17 Oct 2004 (20041017/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l5
L6 14 L5

L6 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:208378 CAPLUS
DN 134:258984
TI Fluorescent maleimides and uses thereof
IN Kunimoto, Kazuhiko; Otani, Junji; Kodama, Kunihiko; Yamamoto, Hiroshi; Verhoustraeten, Patrick; Megert, Sonia; Braig, Adalbert
PA Ciba Specialty Chemicals Holding Inc., Switz.
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001019939	A1	20010322	WO 2000-EP8751	20000907
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6258954	B1	20010710	US 2000-643594	20000822
	BR 2000014089	A	20020521	BR 2000-14089	20000907
	EP 1216285	A1	20020626	EP 2000-965940	20000907
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003509441	T2	20030311	JP 2001-523711	20000907
	US 2002065422	A1	20020530	US 2001-861950	20010521
	US 6508957	B2	20030121		
	US 2003189191	A1	20031009	US 2002-268493	20021010
PRAI	EP 1999-810826	A	19990916		
	US 2000-643594	A3	20000822		
	WO 2000-EP8751	W	20000907		
	US 2001-861950	A3	20010521		

OS MARPAT 134:258984
AB Maleimide derivs. and methods for producing them by reacting maleic anhydride derivative and an amine are described. Use of maleimide derivs. as UV fluorescent materials for void detection and for the preparation of scintillator films, luminescent solar energy collectors, organic electroluminescent devices, printing inks, non-impact printing inks, electrophotog. toners, color filters, and colored high mol. organic materials is also described.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:474298 CAPLUS
DN 131:242780
TI Electrophilic and Nucleophilic Reactivities of the Azomethine Carbon of SAMP-Hydrazones: Stereoselective Synthesis of γ-Amino Ketone Derivatives
AU Enders, Dieter; Diez, Elena; Fernandez, Rosario; Martin-Zamora, Eloisa; Munoz, Jesus M.; Pappalardo, Rafael R.; Lassaletta, Jose M.
CS Departamento de Quimica Organica, Universidad de Sevilla, Seville, E-41071, Spain
SO Journal of Organic Chemistry (1999), 64(17), 6329-6336
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society

DT Journal
LA English
OS CASREACT 131:242780
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A novel methodol. for the asym. synthesis of secondary N-Boc-protected γ-amino ketones is described. Hydrazones such as I (RR1 = O), prepared from the diastereoselective addition of the SAMP-hydrazone of formaldehyde [SAMP = (S)-α-methoxymethylpyrrolidinyl] to α,β-unsatd. ketones, are converted to ethylene ketals such as I (RR1 = OCH2CH2O). Diastereoselective addition of either methyllithium or methylmagnesium bromide to hydrazones such as I gives unstable hydrazines which may either be acylated with methoxycarbonyl chloride to provide hydrazines such as II in 62-81% yields and 62-93% de, or which may be reduced with Raney nickel in methanol and acylated with Boc anhydride to give Boc-protected amines such as III in 30-75% yields and >3:1 diastereoselectivities. E.g., addition of methyllithium to I (RR1 = OCH2CH2O) at -78° in THF followed by acylation with MeOCOCl gives the protected hydrazine II in 65% yield and as a 94:6 ratio of diastereomers. E.g., addition of methyllithium to I (RR1 = OCH2CH2O) in THF, reductive cleavage of the hydrazine with Raney nickel in methanol, and protection of the free amine with Boc anhydride and triethylamine in methanol gives III in 65% yield and as a 93:7 mixture of diastereomers. The azomethine carbon of SAMP-hydrazones, not being essentially modified during the process, sequentially serves as a nucleophilic and an electrophilic center, acting as a nexus between the conjugated enone (electrophile) and the organometallic reagent (nucleophile) and helping in the creation of two adjacent stereogenic centers. Chalcone derivs. such as IV are not effective in this transformation, undergoing acid-catalyzed cyclization instead of ketal formation to give pyrrole derivs. such as V. IV was cleaved with 1,2-ethanedithiol and boron trifluoride etherate to give ketal VI in 90% yield. Complexes of starting methyllithium complexes with SAMP hydrazones, a proposed transition state, and a product complex are modeled by ab initio calcns.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:523272 CAPLUS
DN 127:255115
TI Magnetic field effect on photochromism. Recombination of 2,3,4,5-tetraphenylpyrrolyl radicals
AU Nakai, Takako; Tani, Masanao; Nishio, Satoru; Matsuzaki, Akiyoshi; Sato, Hiroyasu
CS Department of Chemistry for Materials, Faculty of Engineering, Mi'e University, Tsu, 514, Japan
SO Chemistry Letters (1997), (8), 795-796
CODEN: CMLTAG; ISSN: 0366-7022
PB Chemical Society of Japan
DT Journal
LA English
AB Photochromism of the dimer of 2,3,4,5-tetraphenylpyrrolyl radical consists of coloration by photochem. scission and decoloration by thermal recombination of radicals. Application of external magnetic field gave a pronounced retarding effect on the second-order recombination rate constant of escaped radicals.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

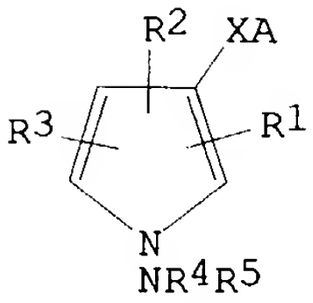
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:53076 CAPLUS
DN 124:201933
TI Synthetic Application of Monoprotected Hydrazines toward the Synthesis of 1-Aminopyrroles
AU McLeod, Matt; Boudreault, Nicolas; Leblanc, Yves
CS Merck Frosst Centre for Therapeutic Research, Pointe Claire-Dorval, QC, H9R 4P8, Can.
SO Journal of Organic Chemistry (1996), 61(3), 1180-3
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
AB Monoprotected hydrazines were condensed with 1,4-dicarbonyl compds. to provide protected 1-aminopyrroles. The hydrazides were then deprotected, under very mild conditions, to provide 1-aminopyrroles. Unsym. 1,1'-bipyrroles and pyrrolylaminopiperidines were then prepared from these 1-aminopyrroles.

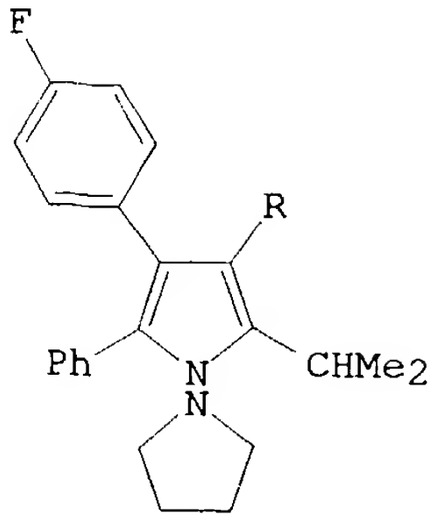
L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:515074 CAPLUS
DN 113:115074
TI Preparation of 5-[(1-piperidinopyrrol-3-yl)vinyl]mevalonates and analogs as HMG-CoA reductase inhibitors
IN Angerbauer, Rolf; Huebsch, Walter; Fey, Peter; Bischoff, Hilmar; Petzinna, Dieter; Schmidt, Delf; Thomas, Guenter
PA Bayer A.-G., Fed. Rep. Ger.
SO Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 339342	A1	19891102	EP 1989-106241	19890408
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
	DE 3813776	A1	19891102	DE 1988-3813776	19880423
	NO 8901480	A	19891024	NO 1989-1480	19890411
	US 4988711	A	19910129	US 1989-337001	19890412
	AU 8933123	A1	19891026	AU 1989-33123	19890418
	FI 8901892	A	19891024	FI 1989-1892	19890420
	JP 01313460	A2	19891218	JP 1989-100322	19890421
	ZA 8902948	A	19891227	ZA 1989-2948	19890421
	DD 283808	A5	19901024	DD 1989-327859	19890421
	HU 53609	A2	19901128	HU 1989-1941	19890421
	CN 1037145	A	19891115	CN 1989-102670	19890422
	DK 8901963	A	19891024	DK 1989-1963	19890424
PRAI	DE 1988-3813776		19880423		
	IT 1988-22264		19881011		

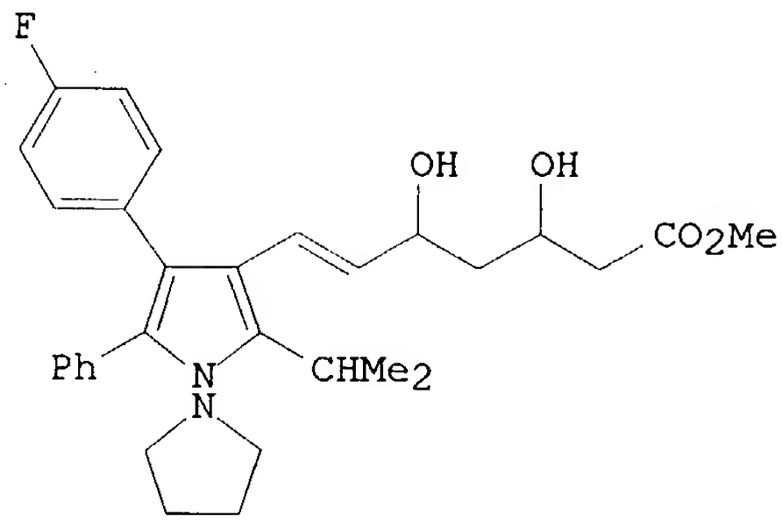
OS CASREACT 113:115074; MARPAT 113:115074
GI



I



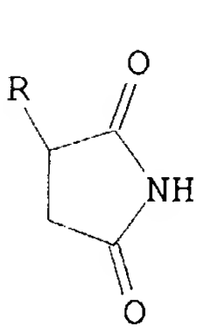
II



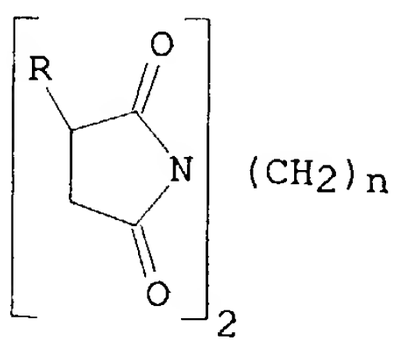
III

AB The title compds. [I; A = CH(OH)CH2CR10(OH)CH2CO2R11; R1 = cycloalkyl, (un)substituted alkyl; R2 = (un)substituted aryl, heteroaryl; R3-R5 = H, cycloalkyl, (un)substituted alkyl, aryl, heteroaryl; NR4R5 = heterocyclyl; R10 = H, alkyl; R11 = H, alkyl, aryl, aralkyl, cation; X = CH2CH2, CH:CH] were prepared as HMG-CoA reductase inhibitors (no data). Thus, 4-FC6H4CH(COPh)CH2COCHMe2 (preparation given) was refluxed 48 h with N-aminopyrrolidine.HCl in DMF containing 3A mol. sieves to give pyrrolidinopyrrole II (R = H) which was refluxed overnight with Me2NCH:CHCHO in MeCN/POCl3 to give II [R = (E)-CH:CHCHO]. The latter was stirred 30 min with MeCOCH2CO2Me in THF which had been treated successively with NaH and BuLi and the product reduced with Et3B/NaBH4 to give erythro-III.

L6 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:486102 CAPLUS
DN 109:86102
TI Succinimide derivatives: chemical structure-anticonvulsant activity relation
AU Avetisyan, S. A.; Nesunts, N. S.; Buyukyan, N. S.; Mndzhoyan, O. L.; Dzhagatspanyan, I. A.; Nazaryan, I. M.; Akopyan, N. E.
CS Inst. Tonkoi Org. Khim. im. Mndzhoyana, Yerevan, USSR
SO Khimiko-Farmatsevticheskii Zhurnal (1988), 22(4), 433-8
CODEN: KHFZAN; ISSN: 0023-1134
DT Journal
LA Russian
OS CASREACT 109:86102
GI



I



II

AB Succinimides (I, R = 4-isopropylphenyl, or 4-cyclopropylphenyl) were prepared by the conversion of the corresponding benzyl chlorides to aldehydes, Knoevenagel reaction with di-Et malonate, HCN addition to the resulting ylidene malonates, hydrolysis, amidation-hydrolysis and cyclization. Treatment of I (R = 4-isopropoxyphenyl) with N2H4 gave N,N'-bis(p-isopropoxyphenylsuccinimide) (II, R = p-isopropoxyphenyl, n = 0). Similarly, other II (R = p-isopropoxyphenyl and n = 1-10) were prepared Of all the compds. studied, I (R = 4-isopropylphenyl, or 4-cyclopropylphenyl) and II (R = 4-isopropoxyphenyl and n = 0, 1, 2, 3, or 4) were completely devoid of the ability to prevent nicotinic hyperkinesis and arecoline tremors, as shown in mice. However, I and pufamide showed anticonvulsant activity in relation to corazole and elec. shock. Antagonism to corazole was observed in 50% of the animals at 68 and 90 mg/kg for I (R = 4-isopropylphenyl and 4-cyclopropylphenyl), resp., and to elec. shock at doses 92 and 94 mg/kg. Structure-activity relations are discussed.

L6 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1972:513682 CAPLUS
DN 77:113682
TI Conformations of substituted N,H'-diacylaminosuccinimides
AU Foucaud, Andre; Roudaut, Rene; Fayat, Christian
CS Groupe Rech. Physicochim. Struct., Univ. Rennes, Rennes-Beaulieu, Fr.
SO Bulletin de la Societe Chimique de France (1972), (5), 1915-20
CODEN: BSCFAS; ISSN: 0037-8968
DT Journal
LA French
GI For diagram(s), see printed CA Issue.
AB Potential barriers to rotation for succinimides (I and II) were 19 kcal/mole and 23 kcal/mole, resp. The conformations of several other succinimides were examined by ir and NMR methods.

L6 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1970:132121 CAPLUS
DN 72:132121
TI Thermocatalytic isomerization of 1-formyl-2,3-diphenylcyclopropene and its corresponding azine
AU Komendantov, M. I.; Kryuchkova, I. K.; Domnin, I. N.
CS Leningrad. Gos. Univ. im. Zhdanova, Leningrad, USSR
SO Zhurnal Organicheskoi Khimii (1970), 6(3), 731-2
CODEN: ZORKAE; ISSN: 0514-7492
DT Journal
LA Russian
AB Heating 1-formyl-2,3-diphenyl-2-cyclopropene (I) with the catalytic amount of Cu stearate (II) at 80° gave quant. yield of 2,3-diphenylfuran. The reaction of I with H2NNH2.H2O gave the corresponding azine which on heating with II isomerized to 2,3,2',3'-tetraphenyl-N,N'-bipyrr ole. A sigmatropic mechanism (G. B. Gille, 1968) is proposed for these 2 isomerizations.

L6 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1968:486741 CAPLUS
DN 69:86741
TI Phenylbutyrolactone derivatives. III. Synthesis of potential antiinflammatory agents related to 3,3'-diphenyl-N,N'-dipyrrolidine-2,2'-dione. I
AU Cignarela, G.; Fontanella, L.; Aresi, V.; Testa, E.
CS Lab. Ric., "Lepetit" S.p.A., Milan, Italy
SO Farmaco, Edizione Scientifica (1968), 23(4), 321-43
CODEN: FRPSAX; ISSN: 0430-0920
DT Journal

LA Italian
OS CASREACT 69:86741
GI For diagram(s), see printed CA Issue.
AB A number of derivs. of 3,3'-diphenyl-N,N'-dipyrrolidine-2,2'-dione (I) with potential antiinflammatory properties were synthesized. A series of substituted γ-butyrolactones (II) were obtained from the corresponding aminobutyric acids. Thus, 100 g. β-phenyl-β-cyanopropionic acid in 2 l. AcOH was treated with H at room temperature at 20 atmospheric over 50 g. Pd/C to yield 55% γ-phenyl-β-aminobutyric acid (III), m. 220-1° (H2O). A solution of 55 g. III in 400 ml. 50% aqueous AcOH was diazotized at -5° with 42 g. NaNO2 in 110 ml. H2O, and the mixture stirred 1 hr. and worked up to yield 37% β-phenyl-γ-butyrolactone, b0.4 120-2°, m. 43-5° (petroleum ether) and a small amount of 3-benzyl-β-propiolactone (IV), b0.5 108-10°. Treatment of IV with NaH yielded γ-phenyl-β-hydroxybutyric acid (V). Reduction of Et γ-phenylacetoacetate with NaBH4 also gave V. Condensation of Et α-cyanohexanoate (VI) with bis(β-chloroethoxy)methane (VII) gave α-butyl-γ-butyrolactone (VIII). Thus, 372 g. VI was added dropwise at 0° to a solution of 2.2 g. atoms Na in 3 l. EtOH, 173 g. VII added, and the mixture refluxed 4 hrs. and worked up to yield 54% bis(3-cyano-3-carbethoxy-n-heptyloxy)methane (IX), b0.4 195-200°. IX (250 g. in 1 l. EtOH) was treated with 100 ml. concentrated HCl and 500 ml. H2O, and the mixture refluxed and worked up to give 57% VI. To a solution of 25.3 g. Na in 1 l. liquid NH3 97 g. capronitrile was added, the mixture stirred 30 min. and treated with 137 g. BuBr, NH3 slowly evaporated, and 500 ml. Et2O added and the mixture refluxed 2 hrs. and worked up to yield 67% dibutylacetonitrile (X), b25 120-2°. X was condensed with VII and the reaction product hydrolyzed to yield α,α-dibutyl-γ-butyrolactone (XI). Thus, 89 g. X was added to a suspension of 25 g. NaNH2 in 500 ml. toluene, the mixture stirred 30 min., 50 g. VII added, and the mixture refluxed 2 hrs. and worked up, to yield 51% XI, b0.5 106-10°. Similarly prepared were the following γ-butyrolactones (XII) (R, R1, R2, R3, b.p., and % yield given): H, H, Ph, H, b0.4 120-2° (m. 43-5°), 37; H, H, H, Ph, b0.6 118-20° (m. 36-8°), 80; Bu, H, H, H, b0.5 102°, 57; and Bu, Bu, H, H, b0.5 106-10°, 51. Several Br(CH2)mCRR1(CH2)nCO2H (XIII) were prepared Thus, a solution of 0.2 ml. of the appropriate XII in 150 ml. AcOH was saturated with anhydrous HBr at 5°, and the mixture heated 2 hrs. at 80°, let stand, and worked up to give XIII [R, R1, m, n, m.p., b.p. of the Cl analog (prepared by refluxing XIII 3-5 hrs. in SOCl2-CHCl3), and % yield of XIII and its Cl analog given]: Ph, H, 1, 1, 93-5° (ligroine), b0.8 115-17°, 74, 94; Ph, H, 0, 2, 74-6° (ligroine), - (decomposed), 77, 98; Bu, H, 2, 0, b0.6 128-32°, - (b2 93-7°), 70.5, 85; Bu, Bu, 2, 0, -, b0.4 118-22°, 90, 82; and Ph, H, 3, 0, 85-6° (ligroine), b0.4 117-20°, 80, 74. A number of N,N'-bis(ω-bromoacyl)hydrazines [Br(CH2)mCHR(CH2)nCONH]2 (XIV) were prepared Thus, a solution of 0.1 mole XIII in 50 ml. Et2O (or C6H6) was added dropwise at 5° to 0.22 mole N2H4.H2O in H2O, and the mixture stirred vigorously, left at room temperature 1 hr., and worked up. The following XIV were prepared (R, m, n, m.p., and % yield given): Ph, 1, 1, 133-7°, 88; Et, 0, 2, 128-30°, 50; Bu, 2, 0, 185-8°, 77; and Ph, 3, 0, 204-5°, 82. A suspension of 15 g. N,N'-bis(β-phenyl-γ-bromobutyryl)hydrazine in 70 ml. EtOH was treated with aqueous 10% NaOH at 5-10°, pH adjusted to 5-6 with dilute aqueous HCl, and the solution worked upto give XV (R = R1 = H, R3 = R2 = Ph). The following XV were prepared (R, R1, R2, R3, and b.p. or m.p. given): H, H, Ph, H, 146-7° (EtOH); H, H, H, Ph, 195-6° (EtOH); H, H, H, Ph, 123-4° (EtOH); Bu, H, H, H, b0.6 165-8°; Bu, Bu, H, H, b0.4 158-63°; and cyclohexyl, H, H, H, 160-2° (ligroine). To a solution of 0.03 mole 1-amino-3-phenylpyrrolidin-2-one and 0.03 mole Et3N in 150 ml. Et2O, 0.03 mole of

the appropriate XIV was added dropwise at 5-10°, and the mixture refluxed 2 hrs. and worked up to yield the following XVI (R, R1, R2, and m.p. given): Ph, Et, CH2Br, 104-7° (iso-Pr2O); Ph, Pr, CH2Br, 91-5° (iso-Pr2O); Ph, Bu, CH2Br, 73-5° (iso-Pr2O); iso-Pr, iso-Pr, CH2Br, 131-3° (iso-Pr2O); and Ph, H, (CH2)3, 128-30° (iso-PrOH). A suspension of 15.3 g. N,N'-bis(α-phenyl-δ-bromovaleroyl)hydrazine in 100 ml. EtOH was treated with 40 ml. N NaOH, and the mixture stirred 3 hrs. at room temperature and worked up to yield 2.9 g.

XVII (R = Ph, R1 = H, n = m = 3), m. 198-200° (EtOH), and 3.8 g. diastereomer, m. 157-9° (EtOH), was recovered. The following XVII were similarly prepared (R, R1, n, m, and m.p. given): Ph, Et, 2, 1, 76-9° (iso-Pr2O); Ph, Pr, 2, 1, 81-3° (iso-Pr2O); Ph, Bu, 2, 1, 86-9° (iso-Pr2O); iso-Pr, iso-Pr, 2, 1, 79-80° (EtOH); and Ph, H, 2, 3, 158-60° (EtOH). A solution of 30 g. N-methyl-N-(2-phenylpropionyl)-N'-benzalhydrazine and 2.2 g. PhNHNH2 in 150 ml. EtOH was acidified with a few drops concentrated HCl and refluxed 6 hrs.

to yield 77% 1-(N-methyl-α-phenylpropionamido)-3-phenylpyrrolidin-2-one (XVIII), m. 108-10° (EtOH). A solution of 5 g. α-phenyl-γ-bromobutyric acid in 20 ml. Et2O was added dropwise at 0° to 3.41 g. XVIII in 5 ml. Et3N and 50 ml. Et2O, and the mixture stirred 30 min. at 0°, refluxed 1 hr., and worked up to yield 40% 1-(N-methyl-α-phenylpropionamido)-3-phenylpyrrolidin-2-one, m. 122° (Et2O). A solution of 16 g. MeNHNH2 sulfate was treated with 12 g. KOH in MeOH, filtered, treated with 10 g. Me γ-bromo-α-phenylbutyrate, and the mixture refluxed 15 hrs. and worked up to yield 26.4% 1-methyl-4-phenylhexahydropyridaz-3-one, m. 200-2° (EtOH). Spectroscopic data (ir and N.M.R.) of all new compds. are given. 19 references.

L6 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1966:438389 CAPLUS
DN 65:38389
OREF 65:7125g-h,7126a-d
TI Phenylbutyrolactones. I. 3,3'-Diphenyl-N,N'-dipyrrolidine-2,2'-dione. Separation and chemical behavior of the diastereoisomeric forms
AU Cignarella, G.; Pagliarini, G.; Testa, E.
CS Lab. Ric. Lepetit S.p.A., Milan
SO Farmaco, Edizione Scientifica (1966), 21(5), 370-80
CODEN: FRPSAX; ISSN: 0430-0920
DT Journal
LA Italian
GI For diagram(s), see printed CA Issue.
AB cf. preceding abstract PhCH(CH2CH2Br)COCl (I) (26.1 g.) added at 0° to 10 g. 98% N2H4.H2O in 200 ml. H2O and the mixture stirred 1 hr. at 0° gave 70% [PhCH(CH2CH2Br)CONH]2 (II), m. 189-90° (Me2CO).
To a suspension of 33.6 g. II in 400 ml. EtOH, 56 ml. 10% NaOH was added at room temperature and the mixture stirred until solution, acidified to pH 2, and

diluted with H2O precipitated 75% III as a mixture of diastereoisomers, m. 150-3°, which were isolated as follows: The above mixture (41 g.) crystallized from 600 ml. EtOH gave at room temperature 20.5 g. a compound m. 174-8° which by further crystallization from 400 ml. EtOH gave 14.8 g. the diastereoisomer IIIa, m. 188-90°. The mother liquor of the 1st crystallization, concentrated in vacuo and allowed to stand at room temperature precipitated 12.7 g.
a compound m. 147-51°, which crystallized from 60 ml. EtOH, then from 5 vols. Me2CO gave the diastereoisomer IIIb, m. 158-60°. To confirm the structure, an unambiguous synthesis of III was carried out. Thus, 2.61 g. I added dropwise to a solution of 1.8 g. IV (R = H), 2.02 g. NEt3, and 70 ml. anhydrous Et2O, and the mixture stirred 0.5 hr. gave 73% IV [R =

PhCH(CH2CH2Br)CO], m. 138-40° (dilute EtOH), which (2 g.) in aqueous alc. NaOH at room temperature cyclized to give 1.18 g. a mixture of IIIa and IIIb, from which pure diastereoisomers could be isolated by the above described technique. IIIa and IIIb were stable in refluxing 20% HCl. IIIb kept 2 hrs. in 10% aqueous alc. NaOH was transformed into IIIa. IIIa (10 g.), 27 ml. 10% NaOH and 60 ml. EtOH refluxed 5 hrs., diluted with H2O, the solution concentrated to half volume, unreacted IIIa filtered off, the filtrate adjusted to pH 3, and Et2O added gave 2.75 g. IV [R = PhCH(CO2H)CH2CH2] (V) as a racemic form (Va), m. 150-2° (EtOH). The mother liquor of Va was concentrated to sep. 0.7 g. a 2nd racemic form of V, m. 110-12° (iso-PrOH) (Vb); addnl. 1.2 g. Vb was isolated from the Et2O layer, while the aqueous layer adjusted to pH 4 separated 0.4 g. [PhCH(CO2H)CH2CH2NH]2, m. 154-6° (dilute EtOH). Va refluxed 2 hrs. in PhMe gave 70% IIIb; Vb, similarly treated, gave 85% IIIa. Attempts to sep. the optical antipodes of Va failed. In fact, Va did not give a salt with d-quinine, brucine, and l-ephedrine; the Me ester of Va, m. 109-10°, (from Va with CH2N2 in Et2O) did not give a salt with d-camphorsulfonic acid; the NH2 group of Va did not give a formyl derivative with 98% HCO2H at 100° because a cyclization to IIIb took place. IIIa (4.55 g.) added to 0.66 g. Na in 100 ml. liquid NH3, the mixture stirred 0.5 hr., 6.30 g. MeI added, NH3 allowed to evaporate, 100 ml. Et2O added to the residue, and the mixture refluxed 0.5 hr. gave 3.46 g. VII as a diastereoisomer (VIIa), m. 168-70° (iso-PrOH). IIIb (3.95 g.), similarly treated, furnished a mixture of 1.14 g. VIIa and 0.81 g. of a diastereoisomer m. 115-18° (VIIb), which were separated by crystallization from Me2CO, then from iso-PrOH. VIIa and VIIb refluxed 12 hrs. in 10% aqueous alc. NaOH were recovered

L6 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1966:406506 CAPLUS
DN 65:6506
OREF 65:1224g
TI Relation of structure to action in some cyclic compounds containing phenylethylamine groups
AU Starykh, N. T.; Krylov, S. S.; El'tsov, A. V.; Chigarev, A. G.
SO Farmakologiya i Toksikologiya (Moscow) (1966), 29(1), 25-31
CODEN: FATOAO; ISSN: 0014-8318
DT Journal
LA Russian
AB A group of compds., 2-phenylpyrrolidine and 2-phenylpiperidine derivs., has adrenergic blockade properties and is capable of blocking central H-choline receptors. The adrenergic-blocking activity of 2-phenylpyrrolidine and 2-phenylpiperidine derivs. is due to the presence of the 2-phenylethylamine group in their heterocyclic structure. The blocking activities of 18 of these derivs. are tabulated.

L6 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1966:406505 CAPLUS
DN 65:6505
OREF 65:1224f-g
TI The synthesis and pharmacologic evaluation of 8-alkylthioxanthines and related compounds as potential antitumor agents
AU Goldsmith, Robert Howard
CS Univ. of Maryland, College Park
SO (1966) 115 pp. Avail.: Univ. Microfilms (Ann Arbor, Mich.), Order No. 65-4447
From: Dissertation Abstr. 26(9), 5481
DT Dissertation
LA English
AB Unavailable

L6 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1965:488729 CAPLUS
DN 63:88729
OREF 63:16289g-h,16290a-b
TI Aryl-substituted 1,1'-bipyrryls and their dissociation into radicals
AU Schilffarth, Karlchristian; Zimmermann, Herbert
CS Univ. Munich, Germany
SO Chemische Berichte (1965), 98(10), 3124-32
CODEN: CHBEAM; ISSN: 0009-2940
DT Journal
LA German
GI For diagram(s), see printed CA Issue.
AB A series of octaarylbipyrryls (I) was prepared from the alkali derivs. of the corresponding H with Br. I dissociated in solution with the fornation of deeply colored radicals. The equilibrium between the I and the pyrryls (III) were measured spectroscopically. Anisoin (14-g.) and 30 g. NH4OAc in 300 co. AcOH refluxed 5 hrs. with 3.2 g. Zn dust gave 8.2 g. 2,3,4,5-tetrakis(p-methoxyphenyl)pyrrole, m. 193° (EtOH). p-PhC6H4CH(OH)COC6H4Ph-p (13 g.) and 300 g. NH4OAc in 1.2 l. AcOH refluxed 3 hrs. with 3 g. Zn dust gave 7.5 g. II (Ar = p-PhC6H4) (IV), m. 262° (MePh). II (Ar = Ph) or II (Ar = p-MeOC6H4) (3 millimoles) in 100 cc. dry dioxane refluxed 4 hrs. with about 70 mg.-atom K in small pieces and yielded 100% K derivative of H (Ar = Ph) and 53% K derivative of II (Ar = p-MeOC6H4), resp. BzPh (500 mg.) in O-free C6H6 shaken 5 min. with 100 g. 1% K-Hg and treated with stirring with 1.8 g. IV yielded 1.25 g. K derivative of IV. The appropriate K derivative (3 millimoles) in 50 cc. dry Et2O treated at 0-5° with 2.8 mg.-atom Br in N as a carrier, filtered, concentrated to 10 cc., and diluted with 5 cc. petr. ether gave the corresponding I (Ar, % purity, and m.p. with decomposition given): Ph, 100, 114° pPhC6H4, 80, 180° p-MeOC6H4, 98, 130°. Na derivative (1.5 g.) of II (R = Ph) in 50 cc. dry Et2O treated with 0.6 g. Br, filtered, concentrated to 10 cc., and diluted with 10 cc. petr. ether yielded 0.32 g. yellow 1-bromo-2,3,4,5-tetraphenylpyrrole, m. 70° (decomposition) (1:1 Et2O-petr. ether); it showed photochromic properties. The -log K (dissociation constant), the dissociation enthalpies and entropies in kcal./mole, and the free enthalpies in cal./degree/mole were determined for the following equilibrium I .rdblhar. III (Ar and the thermodynamic data given in the indicated order): Ph, 2.99, 15, 4.1, 37; pPhC6H4, 2.87, 13, 3.9, 31; p-MeOC6H4, 1.6, 7, 2.2, 17. The I are thermochromic in solution as well as in the solid state; they are also photochromic and can be cleaved into III by irradiation. The absorption spectra of III are recorded.

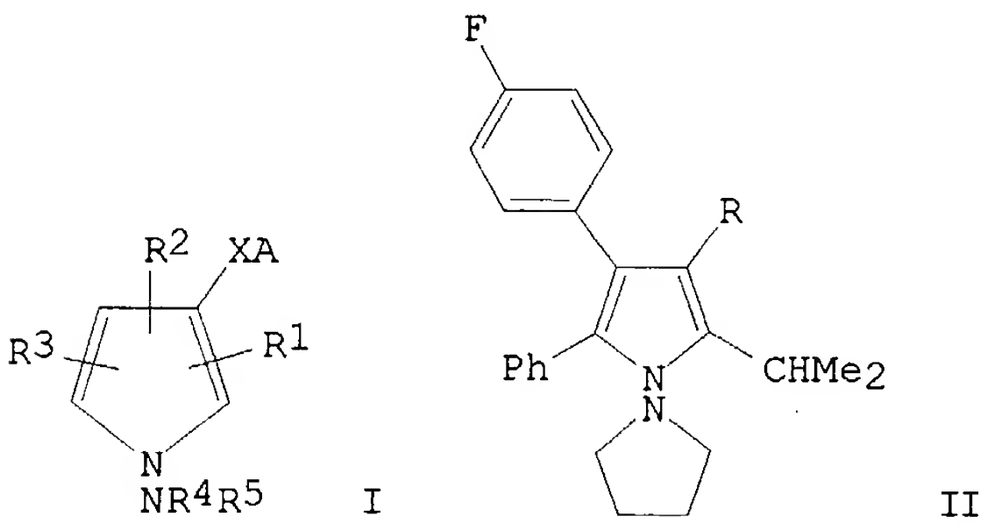
L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1962:456245 CAPLUS
DN 57:56245
OREF 57:11188g-i
TI 1,1'-Bipyrrole, 1,1'-biimidazole and their dissocn, into radicals
AU Zimmerman, Herbert; Baumgaertel, H.; Bakke, F.
CS Tech. Hochsehule, Munich, Germany
SO Angew. Chem. (1961), 73, 808
DT Journal
LA Unavailable
AB Reaction of the K salt of 2,3,4,5-tetra-phenylpyrrole in ether under N with Cl gives 60-80% 1,1'-bi(2,3,4,5-tetraphenylpyrrole) (I). I in solution is in equilibrium with the tetraphenylpyrryl radical as shown by its absolute spectrum. In toluene at 20° the equil, const, is 3.8 + 10-4

mole/l, and ΔH is +14 kcal./mole. Similarly obtained, with iodine in place of Cl, was 1,1'-bi(2,4,5-triphenylimidaz-ole) (II), m. 196°, contg, no active H, also in equil, with its radical. Also prepd, were 1,1'-bi(2-p-tolyl-4,5-diphenyl-imidazole) (III), m. 190° and 1,1'-bi(2-p-methoxyphenyl-4,5-diphenylimidazole) (IV), m. 146°, both of which in solution show equil, with their radicals which are blue to violet in color. The equil, const, k and dissocn, enthalpy H of the imidazoles in toluene are (compound, k, H): II, 0.95 + 10-4 mole/l, at 90°, +19 kcal./mole; III, 1.7 + 10-4 mole/l. at 90°, +15 kcal./mole; IV, 4.6 + 10-4 mole/l, at 60°, +14 kcal./mole.

AN 1990:515074 CAPLUS
DN 113:115074
TI Preparation of 5-[(1-piperidinopyrrol-3-yl)vinyl]mevalonates and analogs as HMG-CoA reductase inhibitors
IN Angerbauer, Rolf; Huebsch, Walter; Fey, Peter; Bischoff, Hilmar; Petzinna, Dieter; Schmidt, Delf; Thomas, Guenter
PA Bayer A.-G., Fed. Rep. Ger.
SO Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

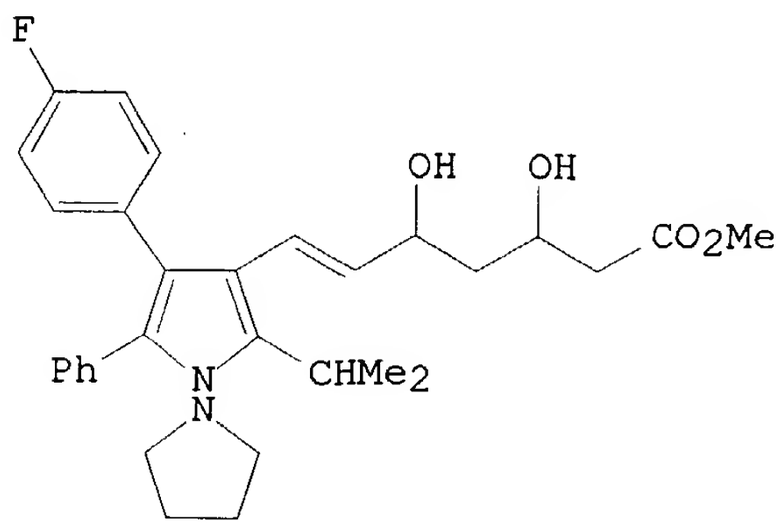
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 339342	A1	19891102	EP 1989-106241	19890408
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
	DE 3813776	A1	19891102	DE 1988-3813776	19880423
	NO 8901480	A	19891024	NO 1989-1480	19890411
	US 4988711	A	19910129	US 1989-337001	19890412
	AU 8933123	A1	19891026	AU 1989-33123	19890418
	FI 8901892	A	19891024	FI 1989-1892	19890420
	JP 01313460	A2	19891218	JP 1989-100322	19890421
	ZA 8902948	A	19891227	ZA 1989-2948	19890421
	DD 283808	A5	19901024	DD 1989-327859	19890421
	HU 53609	A2	19901128	HU 1989-1941	19890421
	CN 1037145	A	19891115	CN 1989-102670	19890422
	DK 8901963	A	19891024	DK 1989-1963	19890424
PRAI	DE 1988-3813776		19880423		
	IT 1988-22264		19881011		

OS CASREACT 113:115074; MARPAT 113:115074
GI



I

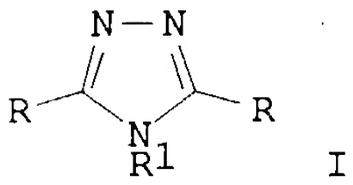
II



III

AB The title compds. [I; A = CH(OH)CH2CR10(OH)CH2CO2R11; R1 = cycloalkyl, (un)substituted alkyl; R2 = (un)substituted aryl, heteroaryl; R3-R5 = H, cycloalkyl, (un)substituted alkyl, aryl, heteroaryl; NR4R5 = heterocyclyl; R10 = H, alkyl; R11 = H, alkyl, aryl, aralkyl, cation; X = CH2CH2, CH:CH] were prepared as HMG-CoA reductase inhibitors (no data). Thus, 4-FC6H4CH(COPh)CH2COCHMe2 (preparation given) was refluxed 48 h with N-aminopyrrolidine.HCl in DMF containing 3A mol. sieves to give pyrrolidinopyrrole II (R = H) which was refluxed overnight with Me2NCH:CHCHO in MeCN/POCl3 to give II [R = (E)-CH:CHCHO]. The latter was stirred 30 min with MeCOCH2CO2Me in THF which had been treated successively with NaH and BuLi and the product reduced with Et3B/NaBH4 to give erythro-III.

AN 1978:6809 CAPLUS
DN 88:6809
TI Synthesis of certain new 4-acylamino-s-triazoles for pharmacological study
AU Amine, F.; El-Zanfally, S.; Khalifa, M.
CS Fac. Pharm., Cairo Univ., Cairo, Egypt
SO Pharmazie (1977), 32(8-9), 538-40
CODEN: PHARAT; ISSN: 0031-7144
DT Journal
LA English
GI

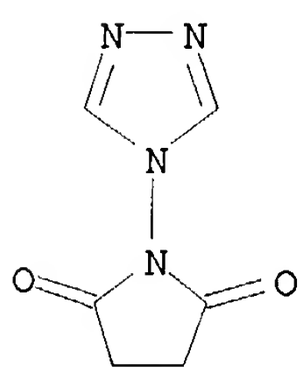


I

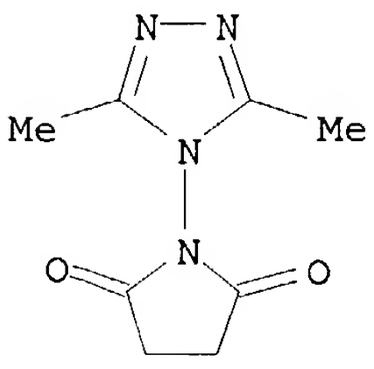
AB Acylaminotriazoles I (R = H, Me; R1 = 4-ClC6H4CONH, 2-ClC6H4CONH, 4-O2NC6H4CONH) were prepared by acylating I (R1 = NH2) with acyl chlorides. I [R = H, Me; R1 = CH2CH2CO2H, CH2CMe2CO2H, CH2CHPhCO2H, CH2C(:CH2)CO2H, (CH2)3CO2H] were similarly prepared by acylation with anhydrides and were cyclized to I (R = succinimido, as-dimethylsuccinimido, phenylsuccinimido, glutarimido, itaconimido).

IT **52782-48-6P 64868-83-3P 64868-84-4P**
64868-85-5P 64868-86-6P 64868-87-7P
64868-90-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 52782-48-6 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(4H-1,2,4-triazol-4-yl)- (9CI) (CA INDEX NAME)

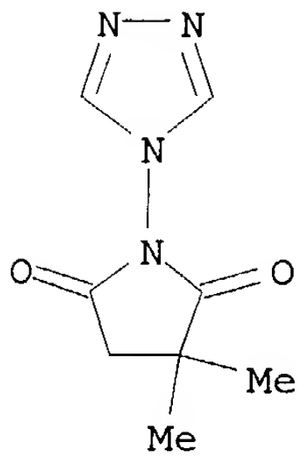


RN 64868-83-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)- (9CI) (CA INDEX NAME)

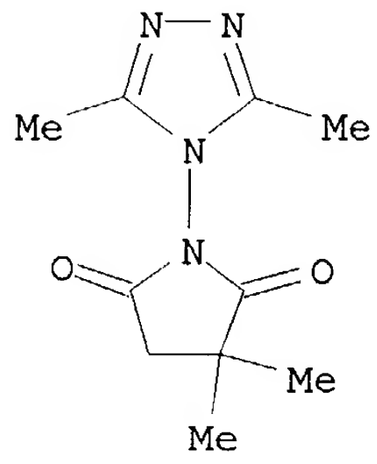


RN 64868-84-4 CAPLUS
CN 2,5-Pyrrolidinedione, 3,3-dimethyl-1-(4H-1,2,4-triazol-4-yl)- (9CI) (CA

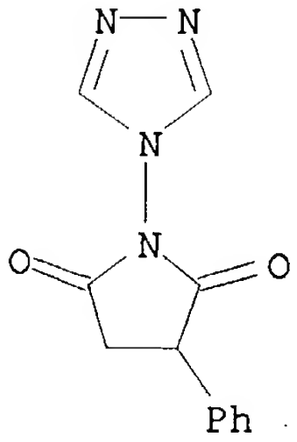
INDEX NAME)



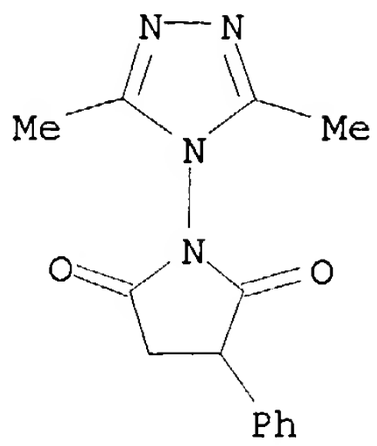
RN 64868-85-5 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)-3,3-dimethyl- (9CI) (CA INDEX NAME)



RN 64868-86-6 CAPLUS
CN 2,5-Pyrrolidinedione, 3-phenyl-1-(4H-1,2,4-triazol-4-yl)- (9CI) (CA INDEX NAME)



RN 64868-87-7 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)-3-phenyl- (9CI) (CA INDEX NAME)



RN 64868-90-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)-3-methylene-
(9CI) (CA INDEX NAME)